Rejection over Guire

The Examiner rejected claims 1-4 and 11 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,263,992 to Guire et al. (the Guire patent). The Examiner indicated that the Guire patent discloses an allograft tissue and that growth factors in the Guire patent are bound covalently with a linker molecule. The Examiner indicated that the linker molecule is a crosslinker molecule.

Applicants submit that amended claim 1 and dependent claims 2-4 and 11 in the present invention are not anticipated by the Guire patent. The disclosure in the Guire patent relates to covalently bonding the growth factors using linker molecules with two different functional groups having a structure denoted as "A-X-B". Furthermore, the linker molecules of the Guire patent are activated sequentially with external activators, such as light and heat. See the Guire patent, col. 5, lines 8-61. The Guire patent stresses the significance of bonding with different functional groups to obtain a desired linked structure. There is no disclosure in the Guire patent regarding covalent bonding of growth factors to tissue using crosslinking agents having functional groups with the same functionalities or using crosslinking agents that are intrinsically active, i.e. do not require activation by an external activator.

Since the Guire patent does not disclose the claimed invention, Applicants respectfully request the withdrawal of the rejection of claims 1-4 and 11 under 35 U.S.C. § 102(b) as being anticipated by the Guire patent.

Rejection over Guire in view of Carpentier

The Examiner rejected claims 5-8, 25, 27 and 28 under 35 U.S.C. 103(a) as being unpatentable over the Guire patent in view of U.S. Patent No. 4,648,881 to Carpentier et al. (The Carpentier patent).

The Examiner indicated that with respect to claims 5, 6, 25, 27 and 28, the Guire patent meets the claim language except for the use of crosslinked or uncrosslinked tissue as a base material. The Examiner stated that the Carpentier patent teaches to use either crosslinked or uncrosslinked tissue as an implant material. The Examiner concluded that it would have been obvious to use the crosslinked or uncrosslinked tissue in the Guire invention.

The Examiner indicated that with respect to claims 7, 8, 27 and 28, the Guire patent meets the claim language but uses human tissue instead of porcine heart valve or bovine pericardial tissue as claimed. The Examiner indicated that the Carpentier patent teaches that it was known to the art to use porcine heart valve or bovine pericardial tissue. The Examiner concluded that it would have been obvious to use either tissue for human tissue of the Guire patent. The Examiner further indicated that it would have been clearly obvious to use crosslinked or uncrosslinked tissue due to its availabiity in the art.

The combination of the Guire patent and the Carpentier patent does not result in the claimed invention as recited in claims 5-8, 25, 27 and 28. With respect to claims 5-8, dependent on amended claim 1, there is no teaching or suggestion in the Guire patent related to use of crosslinking agents having

functional groups with the same functionalities to covalently bond a growth factor to a prosthesis. The Guire patent teaches using linker molecules with photochemical and thermochemical groups to attach a growth factor to a solid surface. As discussed above, the linker molecules include two different functional groups that are sequentially activated. There is no teaching or suggestion in the Carpentier patent related to using crosslinking agents having functional groups with the same functionalities to covalently bond growth factors to tissue. The combination of the Guire patent and the Carpentier patent, thus, does not teach or suggest attaching a growth factor to a prosthesis as claimed in the present invention.

With respect to claims 25, 27 and 28, the combination of the Guire patent and the Carpentier patent does not teach or suggest the claimed invention. There is no discussion in the Guire patent related to attaching growth factors to <u>crosslinked tissue</u>. Crosslinked tissue has specific properties that affect its reactive properties. The Guire patent generally relates to polymer surfaces. The Guire patent merely provides a laundry list of solid surfaces that may be suitable. See the Guire patent, col. 4, lines 2-24. This laundry list, however, does not include <u>crosslinked</u> tissue. It is not inherent based on the polymers in the Guire patent that association of a growth factor with crosslinked tissue will be successful because of the differences between crosslinked tissue and the polymers of the Guire patent.

The Carpentier patent merely indicates the use of crosslinked tissue or uncrosslinked tissue as implantable material. There is no discussion in Carpentier related to

attaching a growth factor. Neither the Guire patent nor the Carpentier patent associate a growth factor with tissue using crosslinking agents such as glutaraldehyde. The Carpentier patent primarily discusses glutaraldehyde treated valves. Attachment of a growth factor to the valve in Carpentier would be undesirable due to the high concentration of glutaraldehyde used in treating the valves of the Carpentier patent. In the present invention, low glutaraldehyde concentrations and/or treatment with ethanol have been included in the protocols used to associate the growth factor with the tissue.

"The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." See MPEP 2143, (emphasis added).

Applicants assert that there is no teaching or suggestion of the claimed invention when the Guire patent and the Carpentier patent are combined. Furthermore, there is no reasonable expectation of success of the claimed invention since the Guire patent provides no guidance for selecting photoactivatable groups to bond with crosslinked tissue. It is only with hindsight that attachment of a growth factor to crosslinked tissue would be expected to be successful.

Applicants submit that independent amended claim 1 and independent claim 25 are not obvious over the Guire patent in view of the Carpentier patent. The dependent claims 5-8, 27 and 28 are thus also not obvious in view of the cited art. Applicants respectfully request the withdrawal of the rejection of claims 5-8, 25, 27 and 28 under 35 U.S.C. § 103(a) as being

unpatentable over the Guire patent in view of the Carpentier patent.

Rejection over Guire and Carpentier further in view of Tischer

The Examiner rejected claims 9, 10, 14, 15, 21-24 and 26 under 35 U.S.C. 103(a) as being unpatentable over the Guire patent and the Carpentier patent further in view of U.S. Patent No. 5,194,596 to Tischer et al. (The Tischer patent).

The Examiner indicated that the Guire patent discloses the use of various growth factors with the implant but fails to disclose the use of vascular endothelial growth factor. The Examiner stated that the Tischer patent teaches the use of vascular endothelial growth factor with implants. The Examiner concluded that it would have been obvious to use vascular endothelial growth factor as the growth factor.

The combination of the Guire patent, the Carpentier patent and the Tischer patent does not teach or suggest the invention claimed in claims 9, 10, amended claim 14, 15, 21-24, and 26. With respect to claims 9 and 10, the combination of the Guire patent and the Carpentier patent does not teach or suggest covalently bonding a growth factor using crosslinking agents as claimed in claims 9 and 10, dependent on amended claim 1. The Tischer patent merely teaches exposing a desired surface to a vascular endothelial growth factor by incubation but does not teach or suggest attachment of the vascular endothelial growth factor using crosslinking agents as claimed in the present invention. Thus, the Tischer patent does not provide any teaching that when combined with the Guire patent and the Carpentier patent results in the claimed invention.

With respect to claims 14, 15 and 21-24, there is no teaching or suggestion when the Guire patent, the Carpentier patent and the Tischer patent are combined regarding attachment of vascular endothelial growth factor to a valve structure as claimed in amended claim 14. There is no guidance in the Guire patent related to selection of appropriate linker molecules for valve structures. The Carpentier patent relates to treatment of tissue and heart valves. There is no discussion in the Carpentier patent related to attachment of growth factors to valve structures. The Tischer patent does not teach or suggest attaching a vascular endothelial growth factor to a valve structure as claimed in the present invention. Applicants submit that incubation with VEGF as discussed in Tischer would not be successful.

With respect to claim 26, there is no teaching or suggestion in any of the cited patents, alone or combined, that vascular endothelial growth factor can be attached to a prosthesis that includes crosslinked tissue. As discussed above, the Guire patent merely provides a laundry list of solid polymer surfaces that may be suitable. See the Guire patent, col. 4, lines 2-24. This laundry list, however, does not include crosslinked tissue. Crosslinked tissue has specific properties that affect its reactive properties. The Carpentier patent does not teach or suggest attaching growth factors to crosslinked tissue. The Tischer patent merely teaches incubation with a vascular endothelial growth factor and not attachment of the vascular endothelial growth factor as in the present invention. The cited patents, alone or combined, do not teach or suggest the invention as claimed in claim 26.

Since the combination of the Guire patent, the Carpentier patent and the Tischer patent does not teach or suggest the claimed invention, Applicants respectfully request the withdrawal of the rejection of claims 9, 10, 14, 15, 21-24 and 26 under 35 U.S.C. § 103(a) as being unpatentable over combination of the Guire patent, the Carpentier patent and the Tischer patent.

CONCLUSIONS

Applicants submit that this application is in condition for allowance, and such action is respectfully requested. The Examiner is invited to telephone the undersigned agent to discuss any questions or comments that the Examiner may have.

The Commissioner is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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